

***REMARKS***

Applicants respectfully request the Examiner to record or note the change of address regarding the Power of Attorney for this application (see also the original Revocation of Power of Attorney of October 7, 2002, copy attached).

***Status of the Claims***

Applicants respectfully request the Examiner to reconsider the present application in view of the foregoing amendments and addition to the claims.

In the present Reply, claims 13-18 have been canceled without prejudice or disclaimer of the subject matter contained therein. Also, claims 1, 3, 6, 7, 9, 10 and 11 have been amended. Further, claim 19 has been added. Thus, claims 1-12 and 19 are pending in the present application.

No new matter has been added by way of these amendments and the new claim, because each amendment and new claim is supported throughout the present specification, including the various Figures and Sequence Listing. For example, the amendments to claims 1, 4 and 9 are supported in the various Figures (e.g., Figure 4) and in the present specification at least at page 6, lines 11-20. With respect to SEQ. ID. NOS. 15 and 16, the most recent version of the Sequence Listing was filed on June 9, 2004. Support for the amendment to claim 7 can be seen on page 7, lines 3-4 of the specification and is merely for clarification purposes. By amending these terms in order to clarify the claimed invention, Applicants are in no way conceding any limitations with respect to the interpretation of the claims under the Doctrine of Equivalents. The amendment to claim 11 has support at least at pages 17-18 of the present specification. Also, new claim 19,

drawn to a preferred embodiment of the present invention, has been added for the Examiner's consideration. Support for new claim 19 can be found in the specification at, e.g., pages 6, 17, 18 and the various Figures. Thus, no new matter has been added.

Based upon the above considerations, entry of the present amendments is respectfully requested.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

***Claim Objections***

Claims 9-10 stand objected to under 37 C.F.R. § 1.75(c) as being in improper form. Applicants respectfully refer the Examiner to the scope of the disputed claims as presented herein. Thus, withdrawal of this objection and consideration of these claims on the merits are respectfully requested.

***Issues Under 35 U.S.C. § 112, Second Paragraph***

Claims 7, 8, 11 and 12 stand rejected under 35 U.S.C. § 112, second paragraph, for asserted reasons of indefiniteness. Applicants respectfully traverse.

With regard to claim 7 and its dependent claims, Applicants respectfully submit that "puro" has been defined in the claim.

With regard to claim 11, the step of trapping the gene has been inserted.

Accordingly, Applicants respectfully submit that this rejection has been overcome. Reconsideration and withdrawal of this rejection are respectfully requested.

***Issues Under 35 U.S.C. § 102***

Claims 1-3 and 11-12 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Araki et al. ("EXCHANGEABLE GENE TRAP USING THE creMUTATED *Lox* SYSTEM," *Cellular and Molecular Biology*, Vol. 45(5), pp. 737-750 (1999)) (see pages 3-4 of the Office Action).

Also, claims 1-3 and 11-12 stand rejected under 35 U.S.C. §102(d) as being anticipated by Ong et al. '235 (U.S. Patent No. 6,777,235) (see page 4 of the Office Action).

Applicants respectfully traverse each and every rejection.

Araki et al.

Applicants submit herewith a certified or verified English translation of the priority document for this application (JP 11/200997, filed July 14, 1999; see also the present specification at page 7, lines 18-20). The JP '997 application fully enables the scope of the pending claims. Thus, the present application has the benefit of priority to the filing date of the JP '997 application. Accordingly, the Araki reference is not prior to the present application.

Further, pursuant to *In re Katz* and M.P.E.P. § 2132.01 (see, e.g., the discussion regarding the *Katz* decision and submission of specific declaration by applicant establishing article is describing applicant's own work), Applicants submit herewith Declarations pursuant to 37 C.F.R. § 1.132 by each of the two inventors. As can be seen from the Rule 132 Declarations, the work in the cited Araki article was derived from Applicants' own work, wherein the co-authors worked under the direction of the present inventors. Thus, this rejection has been sufficiently rebutted.

This rejection is rendered moot for the reasons stated above, and withdrawal thereof is respectfully requested.

Ong '235

The Examiner refers Applicants to column 14, lines 54-55 of Ong '235. However, the vector shown in Figure 4 of Ong '235 fails to disclose a non-mutated *loxP*. Ong '235 fails to disclose or recognize a trap vector which has both wild-type *loxP* and mutant *loxP* sequences. Therefore, the present invention is different, wherein Ong '235 fails to disclose all instantly claimed features. Because "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference," the cited Ong '235 reference cannot be a basis for a rejection under § 102. *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Thus, because of the lack of disclosure of all features as instantly claimed, the rejection in view of Ong '235 is overcome. Reconsideration and withdrawal are respectfully requested.

***Issues Under 35 U.S.C. §103(a)***

Claims 4-6 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Ong '235 (see pages 4-6 of the Office Action). Applicants respectfully traverse and reconsideration and withdrawal of this rejection are respectfully requested.

As mentioned above, the cited Ong '235 reference fails to disclose or recognize a trap vector which has both wild-type *loxP* and mutant *loxP* sequences, wherein the trap vectors in the reference lack a non-mutated *lox* sequence. Thus, this rejection has been overcome since a *prima*

*facie* case of obviousness has not been established. This is because U.S. case law squarely holds that a proper obviousness inquiry requires consideration of three factors: (1) the prior art reference (or references when combined) must teach or suggest all the claim limitations; (2) whether or not the prior art would have taught, motivated, or suggested to those of ordinary skill in the art that they should make the claimed invention (or practice the invention in case of a claimed method or process); and (3) whether the prior art establishes that in making the claimed invention (or practicing the invention in case of a claimed method or process), there would have been a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *see also In re Kotzab*, 55 USPQ2d 1313, 1316-17 (Fed. Cir. 2000); *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995) (“Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination.”). Here, not even the first requirement of disclosure of all claimed features has been satisfied. Further, the Examiner in the Office Action has failed to make up for this deficiency in Ong’s disclosure. Thus, under *Vaeck*, this rejection has been overcome. Reconsideration and withdrawal thereof are respectfully requested.

Further, the Examiner merely states that it would be obvious to exchange *lox71* for *lox66* (see the Office Action in the paragraph bridging pages 5-6). However, the Examiner does not point to any reference supporting this assertion. In this regard, the Examiner has failed to provide any motivation for the exchange, and further has failed to show that the skilled artisan would have a reasonable expectation of success. Applicants note that the teaching or suggestion to make the claimed combination/modification and the reasonable expectation of success must both be found

in the prior art, and not based on applicant's disclosure. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Accordingly, if the Examiner continues to maintain that "using a trap vector having lox66 or lox71 would be interchangeable" (the paragraph bridging pages 5-6 of the Office Action), Applicants hereby challenge this assertion. This challenge is based upon the reasoning above, wherein Applicants request that the Examiner produce evidence to support this assertion with explicit findings on motivation and reasonable expectation of success to select the claimed invention. *See In re Dillon*, 919 F.2d 688, 693, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990)(*en banc*), *cert. denied*, 500 U.S. 904 (1991); *In re Mills*, 680 F.2d 680, 683, 16 USPQ2d 1430, 1433 (Fed. Cir. 1990); *see also* M.P.E.P. § 2144.08(III). Alternatively, if the Examiner is relying upon personal knowledge to support the finding of what is known in the art, the Examiner is respectfully requested to provide an affidavit or declaration setting forth specific factual statements and explanations to support such an assertion. In this regard, the Examiner is referred to 37 C.F.R. § 1.104(d)(2) and *In re Sang Su Lee*, 61 USPQ2d 1430 (Fed. Cir. 2002) (the Federal Circuit held that the Board of Appeals could not merely rely on what is "common-knowledge and common sense" in the art to sustain a rejection under 35 U.S.C. § 103). There was no proper motivation found in the *Lee* case, since the USPTO failed to identify the specific principle known to one of ordinary skill in the art that suggested the claimed method. With regard to motivation or suggestion to select the instantly claimed invention as asserted in the Office Action, Applicants note that any conclusory statements of similarity or motivation, without any articulated rationale or evidentiary support, do not constitute sufficient factual findings. *See*

M.P.E.P. § 2144.08(III). Applicants respectfully submit that the requisite motivation and reasonable expectation of success are lacking. *In re Vaeck*.

Additionally, with regard to the state of the art, one of skill in the art would not do what is asserted in the Office Action. The Examiner asserts that Ong '235 discloses a trap vector comprising a mutant *lox71*, which will recombine with *lox66* in the presence of *Cre*. However, an introduction of mutated *loxP* and wild-type *loxP* is not a standard use of the *Cre-loxP* system. Applicants further submit that a construction of the vector of the present invention is not a common technique for the person of skill in this art. In fact, Applicants submit that the present invention produces unexpected and significant results in that the presently defined trap vectors provide, *viz.*, more efficient production of knock-out organisms, improvements to the detailed analysis of gene function and the enhancement of the production of model organisms for the purposes of disease study (see the present specification at page 32, line 6 to page 33, line 1). In this regard, Applicants further submit that this rejection under § 103(a) is overcome because evidence of unexpected results is in the present specification.

Based on the above, reconsideration and withdrawal of this rejection are respectfully requested.

### ***Conclusion***


A full and complete response has been made to all issues as cited in the Office Action. Applicants have taken substantial steps in efforts to advance prosecution of the present application. Thus, Applicants respectfully request that a timely Notice of Allowance issue for the present case.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Eugene T. Perez (Reg. No. 48,501) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Dated: June 28, 2005

Respectfully submitted,

By   
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Attachments:

- Copy of Revocation of Power of Attorney, Substitute Power of Attorney and Change in Correspondence Address
- Verified English translation of JP 11/200997
- Two (2) Declarations Under 37 C.F.R. § 1.132